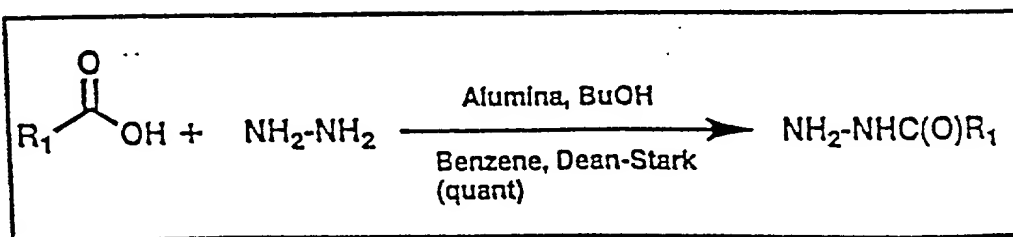
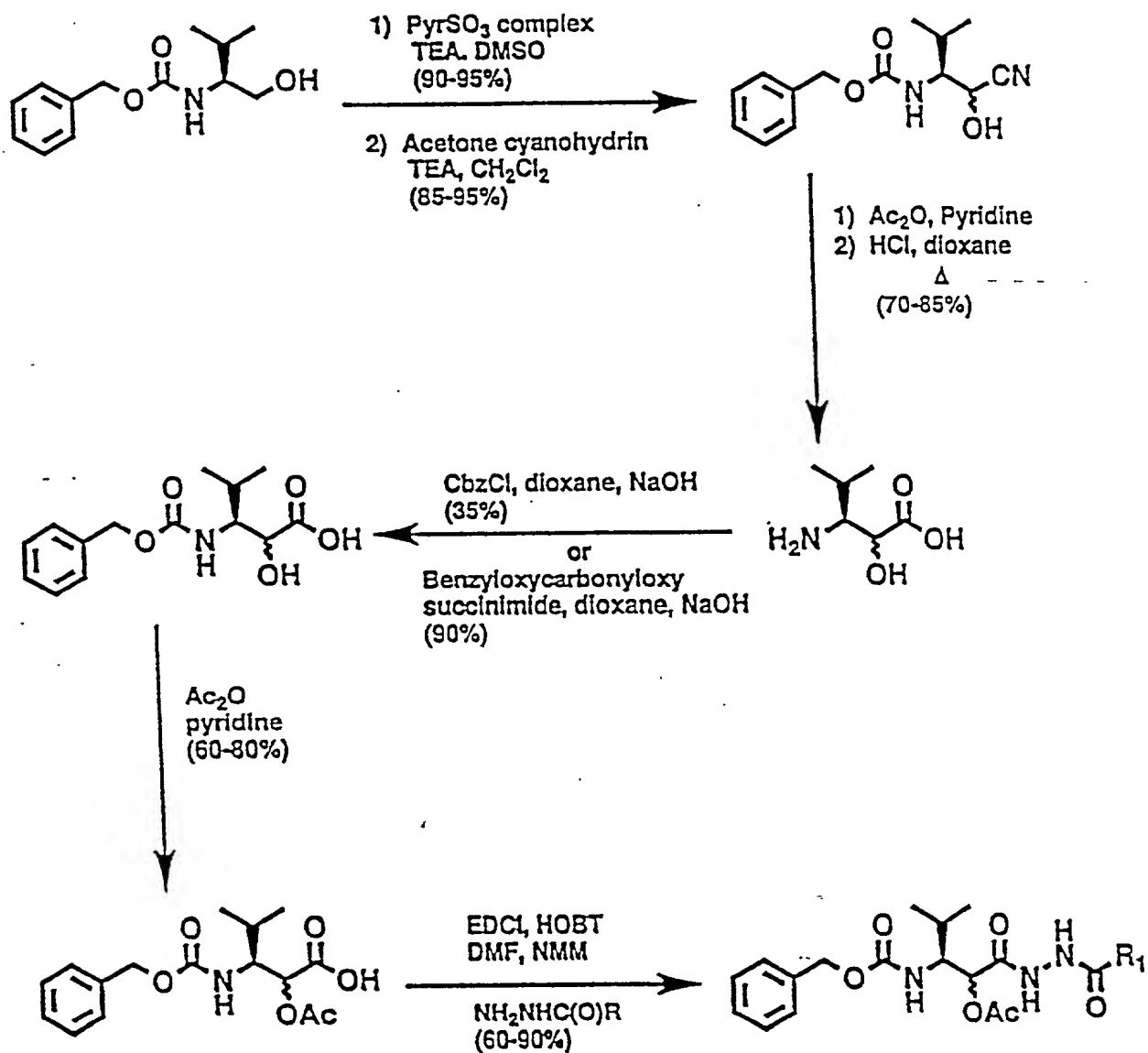


Figure 1

General Synthetic Scheme for 1,3,4-Oxadiazole Inhibitors



T00T80' 22372560

Figure 2

General Scheme for 1,3,4-Oxadiazole Inhibitors - Continued

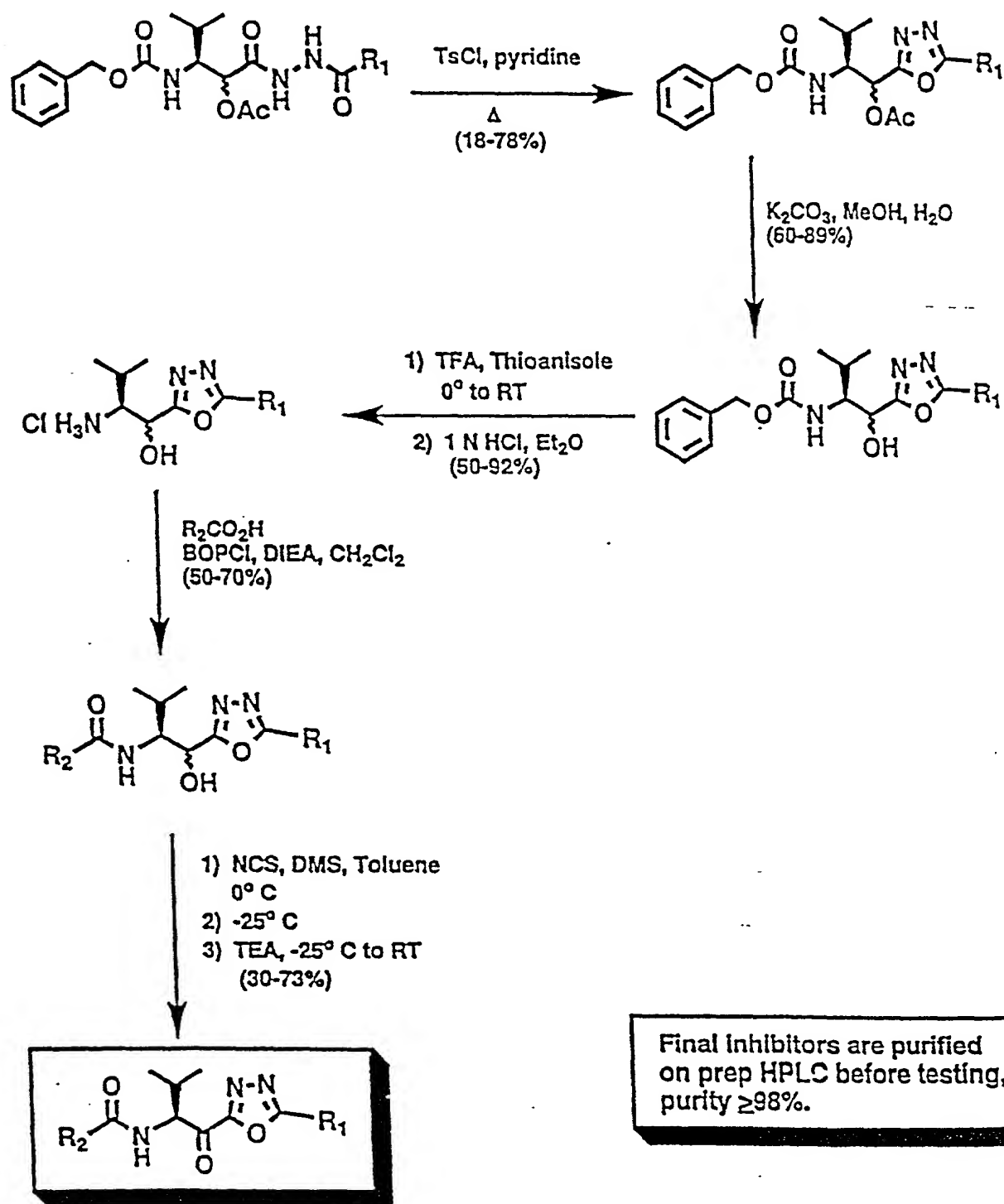
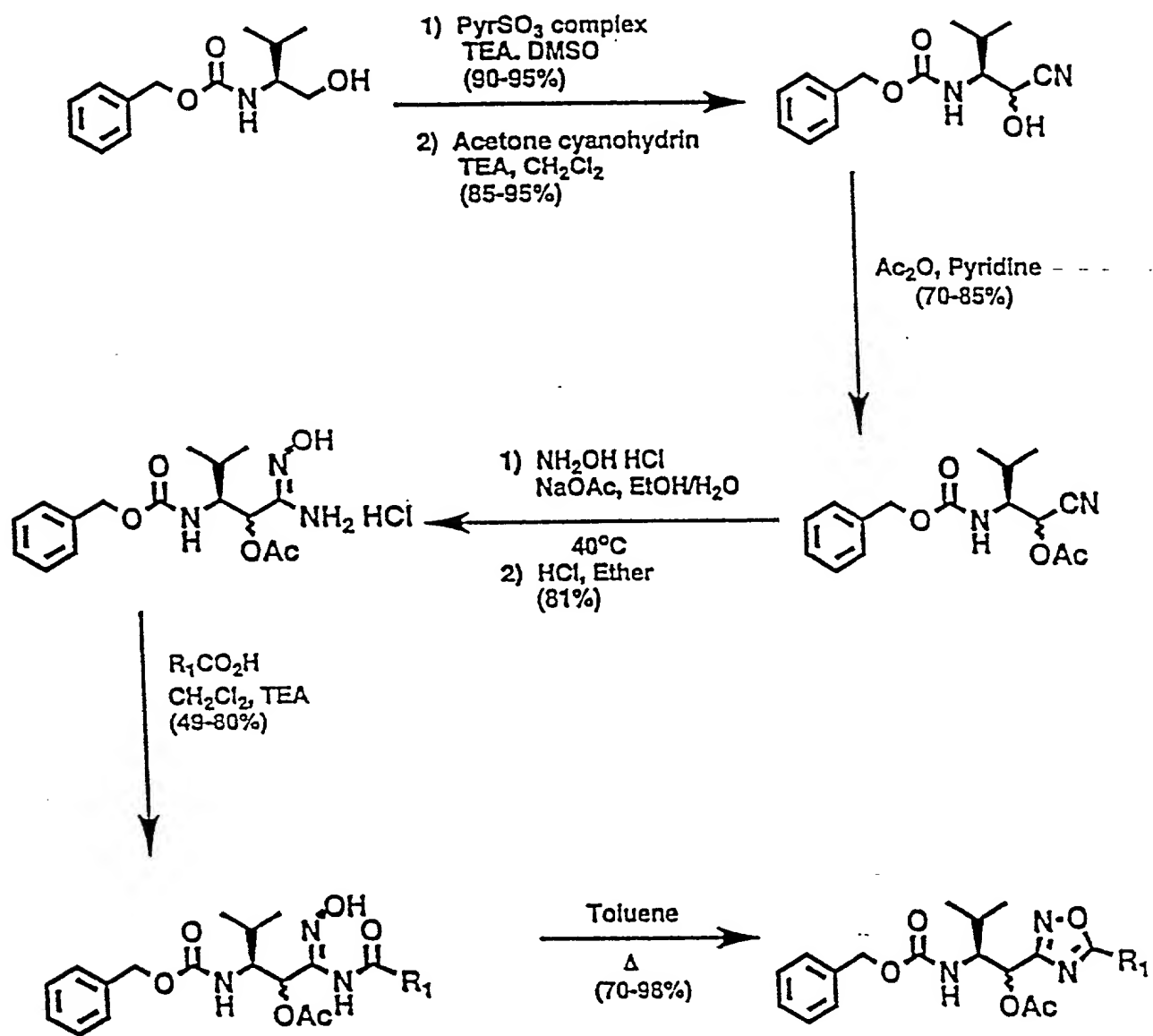


Figure 3

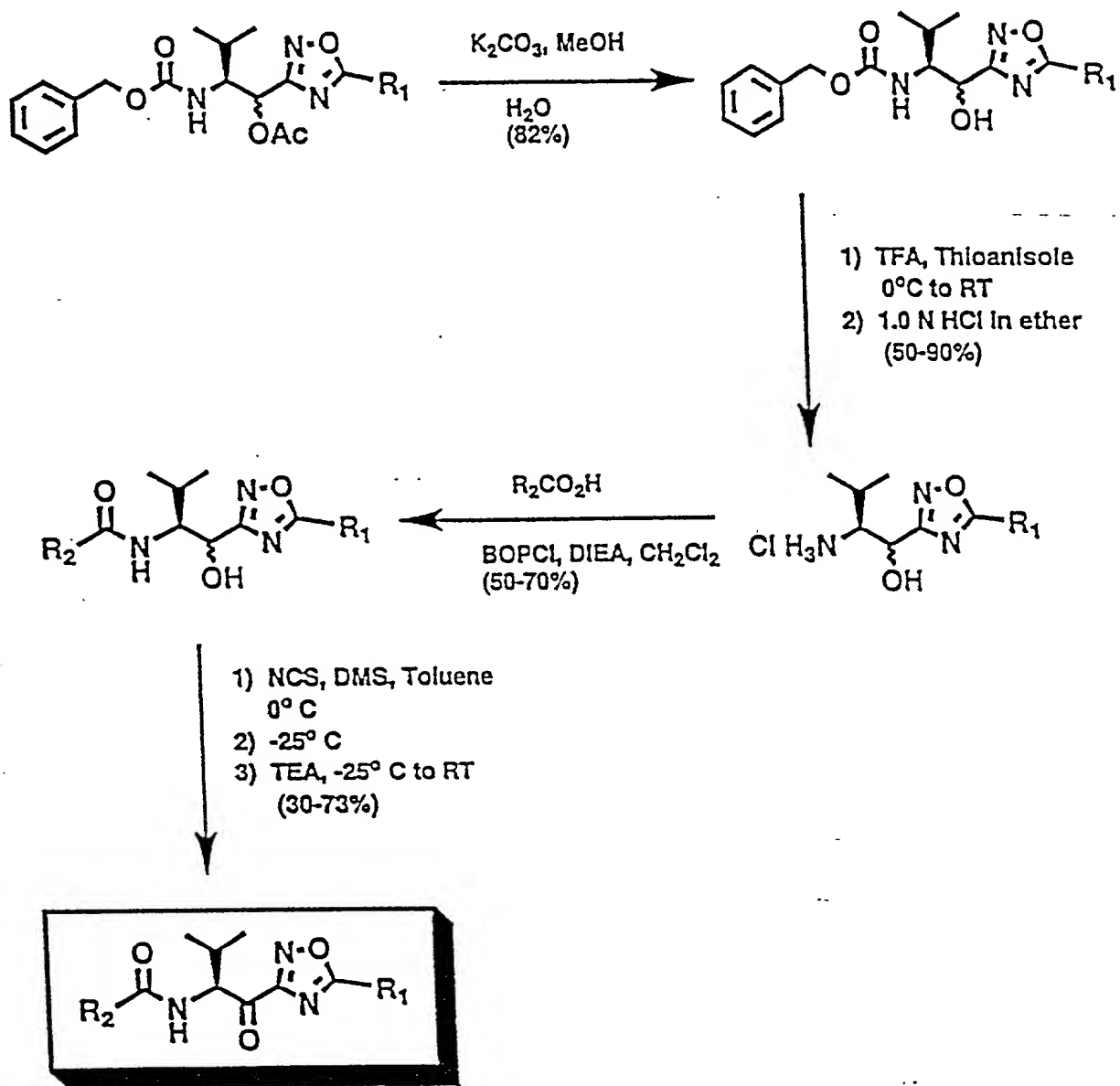
General Synthetic Scheme for 1,2,4-Oxadiazole Inhibitors



100790-222650

Table 1. Demographic characteristics of the study population	
Age (years)	65.8 ± 1.2
Gender (male/female)	10/10
Education (years)	12.5 ± 0.5
Marital status (married/divorced/widowed)	10/0/0
Occupation (retired/employed)	10/0
Income (USD/month)	1,200 ± 100
Smoking status (smoker/non-smoker)	5/5
Alcohol consumption (yes/no)	2/8
Comorbidities (hypertension/diabetes/cholesterol)	8/5/3
Medication (antihypertensive/antidiabetic/anticholesterol)	8/5/3
Physical activity (sedentary/active)	7/3
Stress level (low/moderate/high)	5/5/0
Family history (heart disease/stroke)	3/2
Previous hospitalization (yes/no)	2/8
Current health status (good/fair/poor)	8/2/0
Quality of life (SF-36 score)	45.2 ± 2.1
Depression score (Beck's Depression Inventory)	12.5 ± 1.5
Life satisfaction (satisfied/dissatisfied)	7/3
Healthcare utilization (regular/irregular)	8/2
Health insurance (yes/no)	10/0
Health literacy (high/low)	6/4
Health beliefs (positive/negative)	7/3
Health behaviors (healthy/unhealthy)	6/4
Health outcomes (improved/stable/worsened)	8/2/0
Healthcare costs (low/moderate/high)	5/5/0
Healthcare access (easy/difficult)	7/3
Healthcare quality (good/poor)	8/2
Healthcare satisfaction (satisfied/dissatisfied)	7/3
Healthcare utilization (increased/decreased)	6/4
Healthcare costs (decreased/increased)	6/4
Healthcare access (improved/worsened)	7/3
Healthcare quality (improved/worsened)	8/2
Healthcare satisfaction (improved/worsened)	7/3
Healthcare utilization (stable/unstable)	6/4
Healthcare costs (stable/unstable)	6/4
Healthcare access (stable/unstable)	7/3
Healthcare quality (stable/unstable)	8/2
Healthcare satisfaction (stable/unstable)	7/3
Healthcare utilization (increased/decreased/stable)	6/4/0
Healthcare costs (decreased/increased/stable)	6/4/0
Healthcare access (improved/worsened/stable)	7/3/0
Healthcare quality (improved/worsened/stable)	8/2/0
Healthcare satisfaction (improved/worsened/stable)	7/3/0
Healthcare utilization (increased/decreased/stable/unstable)	6/4/0/0
Healthcare costs (decreased/increased/stable/unstable)	6/4/0/0
Healthcare access (improved/worsened/stable/unstable)	7/3/0/0
Healthcare quality (improved/worsened/stable/unstable)	8/2/0/0
Healthcare satisfaction (improved/worsened/stable/unstable)	7/3/0/0
Healthcare utilization (increased/decreased/stable/unstable/irregular)	6/4/0/0/0
Healthcare costs (decreased/increased/stable/unstable/irregular)	6/4/0/0/0
Healthcare access (improved/worsened/stable/unstable/irregular)	7/3/0/0/0
Healthcare quality (improved/worsened/stable/unstable/irregular)	8/2/0/0/0
Healthcare satisfaction (improved/worsened/stable/unstable/irregular)	7/3/0/0/0
Healthcare utilization (increased/decreased/stable/unstable/irregular/regular)	6/4/0/0/0
Healthcare costs (decreased/increased/stable/unstable/irregular/regular)	6/4/0/0/0
Healthcare access (improved/worsened/stable/unstable/irregular/regular)	7/3/0/0/0
Healthcare quality (improved/worsened/stable/unstable/irregular/regular)	8/2/0/0/0
Healthcare satisfaction (improved/worsened/stable/unstable/irregular/regular)	7/3/0/0/0
Healthcare utilization (increased/decreased/stable/unstable/irregular/regular/consistent)	6/4/0/0/0
Healthcare costs (decreased/increased/stable/unstable/irregular/regular/consistent)	6/4/0/0/0
Healthcare access (improved/worsened/stable/unstable/irregular/regular/consistent)	7/3/0/0/0
Healthcare quality (improved/worsened/stable/unstable/irregular/regular/consistent)	8/2/0/0/0
Healthcare satisfaction (improved/worsened/stable/unstable/irregular/regular/consistent)	7/3/0/0/0
Healthcare utilization (increased/decreased/stable/unstable/irregular/regular/consistent/consistent)	6/4/0/0/0
Healthcare costs (decreased/increased/stable/unstable/irregular/regular/consistent/consistent)	6/4/0/0/0
Healthcare access (improved/worsened/stable/unstable/irregular/regular/consistent/consistent)	7/3/0/0/0
Healthcare quality (improved/worsened/stable/unstable/irregular/regular/consistent/consistent)	8/2/0/0/0
Healthcare satisfaction (improved/worsened/stable/unstable/irregular/regular/consistent/consistent)	7/3/0/0/0
Healthcare utilization (increased/decreased/stable/unstable/irregular/regular/consistent/consistent/consistent)	6/4/0/0/0
Healthcare costs (decreased/increased/stable/unstable/irregular/regular/consistent/consistent/consistent)	6/4/0/0/0
Healthcare access (improved/worsened/stable/unstable/irregular/regular/consistent/consistent/consistent)	7/3/0/0/0
Healthcare quality (improved/worsened/stable/unstable/irregular/regular/consistent/consistent/consistent)	8/2/0/0/0
Healthcare satisfaction (improved/worsened/stable/unstable/irregular/regular/consistent/consistent/consistent)	7/3/0/0/0
Healthcare utilization (increased/decreased/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent)	6/4/0/0/0
Healthcare costs (decreased/increased/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent)	6/4/0/0/0
Healthcare access (improved/worsened/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent)	7/3/0/0/0
Healthcare quality (improved/worsened/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent)	8/2/0/0/0
Healthcare satisfaction (improved/worsened/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent)	7/3/0/0/0
Healthcare utilization (increased/decreased/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent)	6/4/0/0/0
Healthcare costs (decreased/increased/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent)	6/4/0/0/0
Healthcare access (improved/worsened/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent)	7/3/0/0/0
Healthcare quality (improved/worsened/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent)	8/2/0/0/0
Healthcare satisfaction (improved/worsened/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent)	7/3/0/0/0
Healthcare utilization (increased/decreased/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent/consistent)	6/4/0/0/0
Healthcare costs (decreased/increased/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent/consistent)	6/4/0/0/0
Healthcare access (improved/worsened/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent/consistent)	7/3/0/0/0
Healthcare quality (improved/worsened/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent/consistent)	8/2/0/0/0
Healthcare satisfaction (improved/worsened/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent/consistent)	7/3/0/0/0
Healthcare utilization (increased/decreased/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent/consistent/consistent)	6/4/0/0/0
Healthcare costs (decreased/increased/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent/consistent/consistent)	6/4/0/0/0
Healthcare access (improved/worsened/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent/consistent/consistent)	7/3/0/0/0
Healthcare quality (improved/worsened/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent/consistent/consistent)	8/2/0/0/0
Healthcare satisfaction (improved/worsened/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent/consistent/consistent)	7/3/0/0/0
Healthcare utilization (increased/decreased/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent/consistent/consistent/consistent)	6/4/0/0/0
Healthcare costs (decreased/increased/stable/unstable/irregular/regular/consistent/consistent/consistent/consistent/consistent/consistent/consistent/consistent)	6/4/0/0/0
Healthcare access (improved/worsened/stable/unstable/irregular/regular/	

**General Synthetic Scheme for 1,2,4-Oxadiazole inhibitors
(Continued)**



[illegible]

General Synthetic Scheme for P₂-P₃ Modified Based Inhibitors

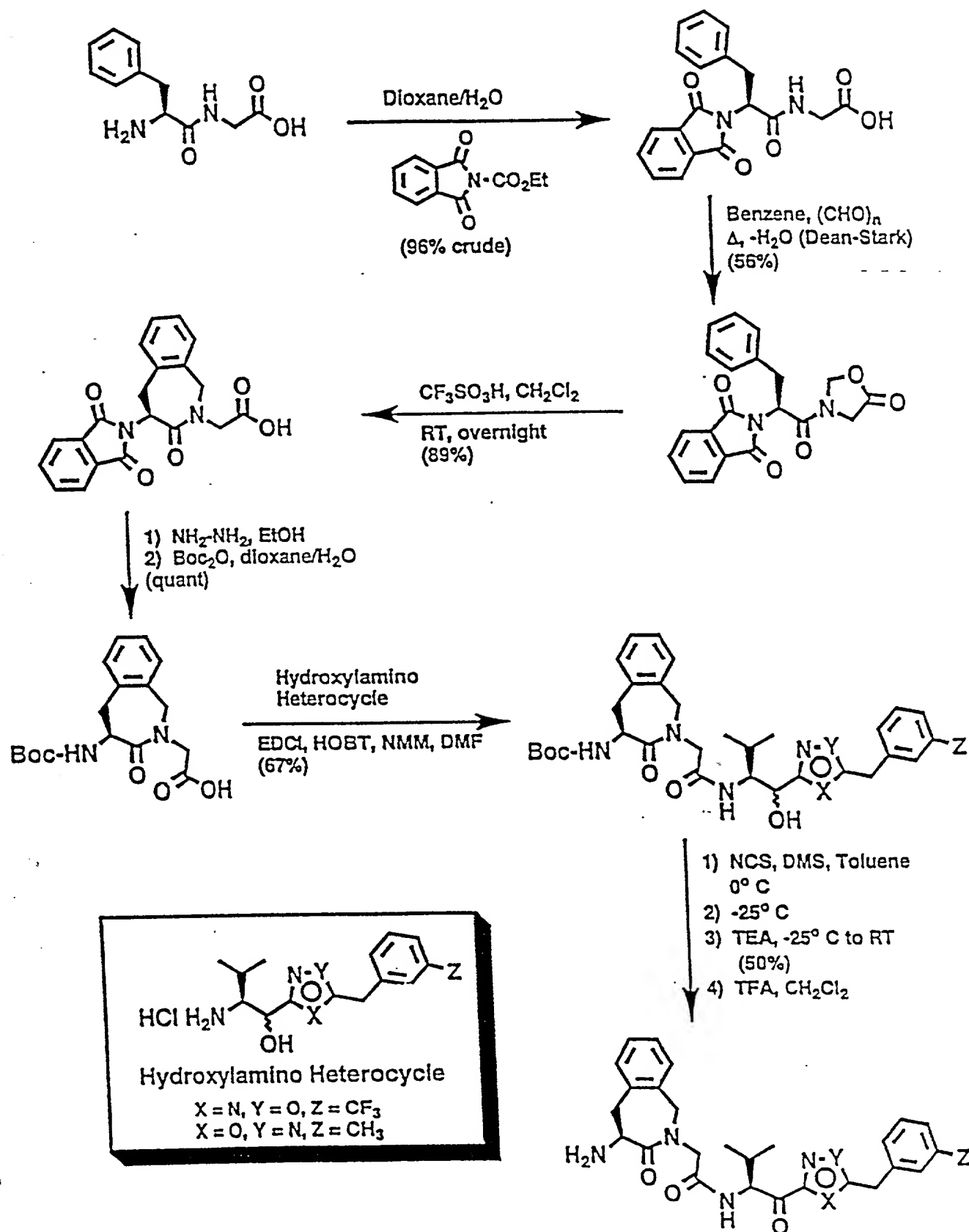


Figure 6

Synthetic Scheme for P₂-P₃ Modified Inhibitors

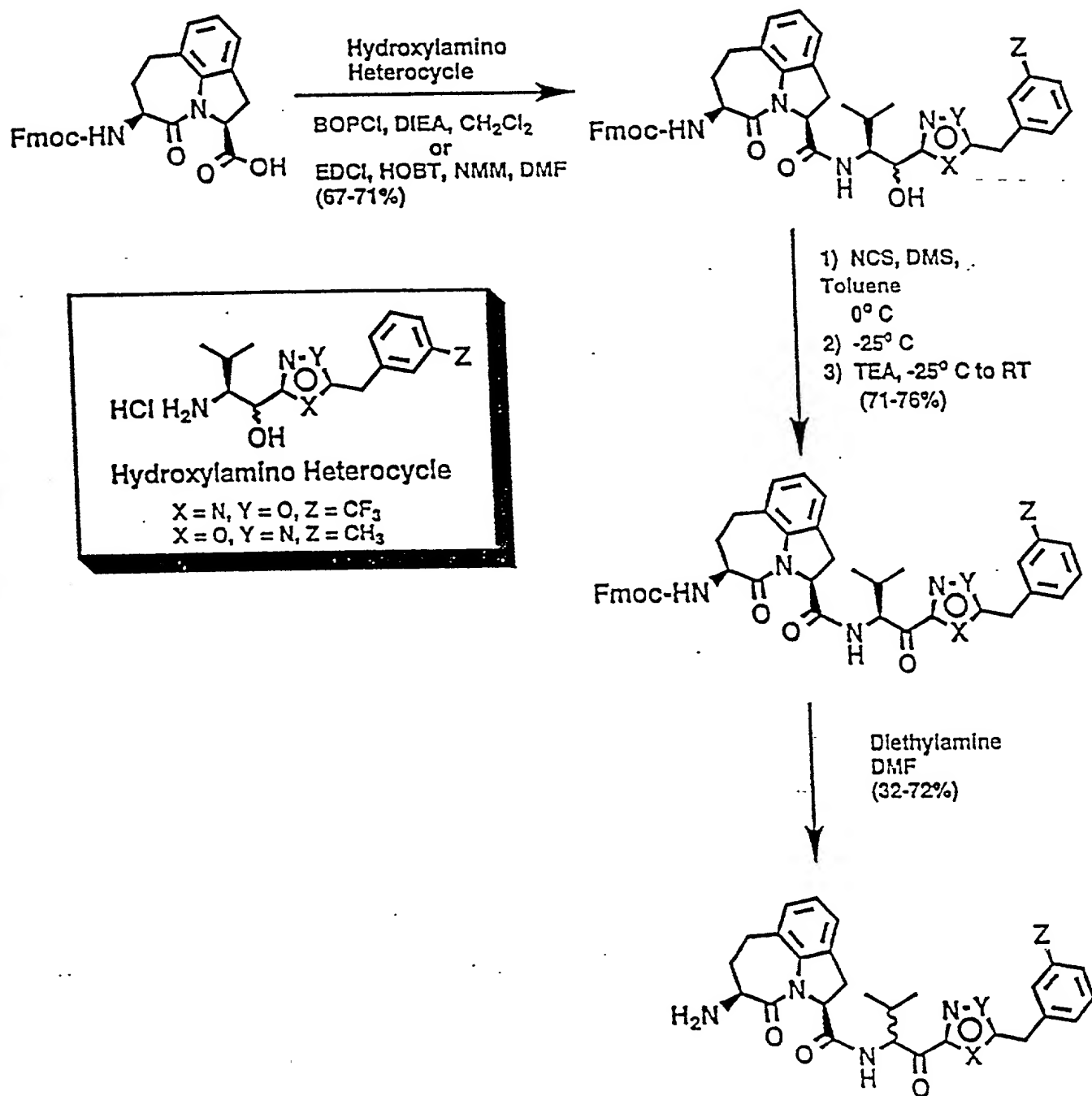
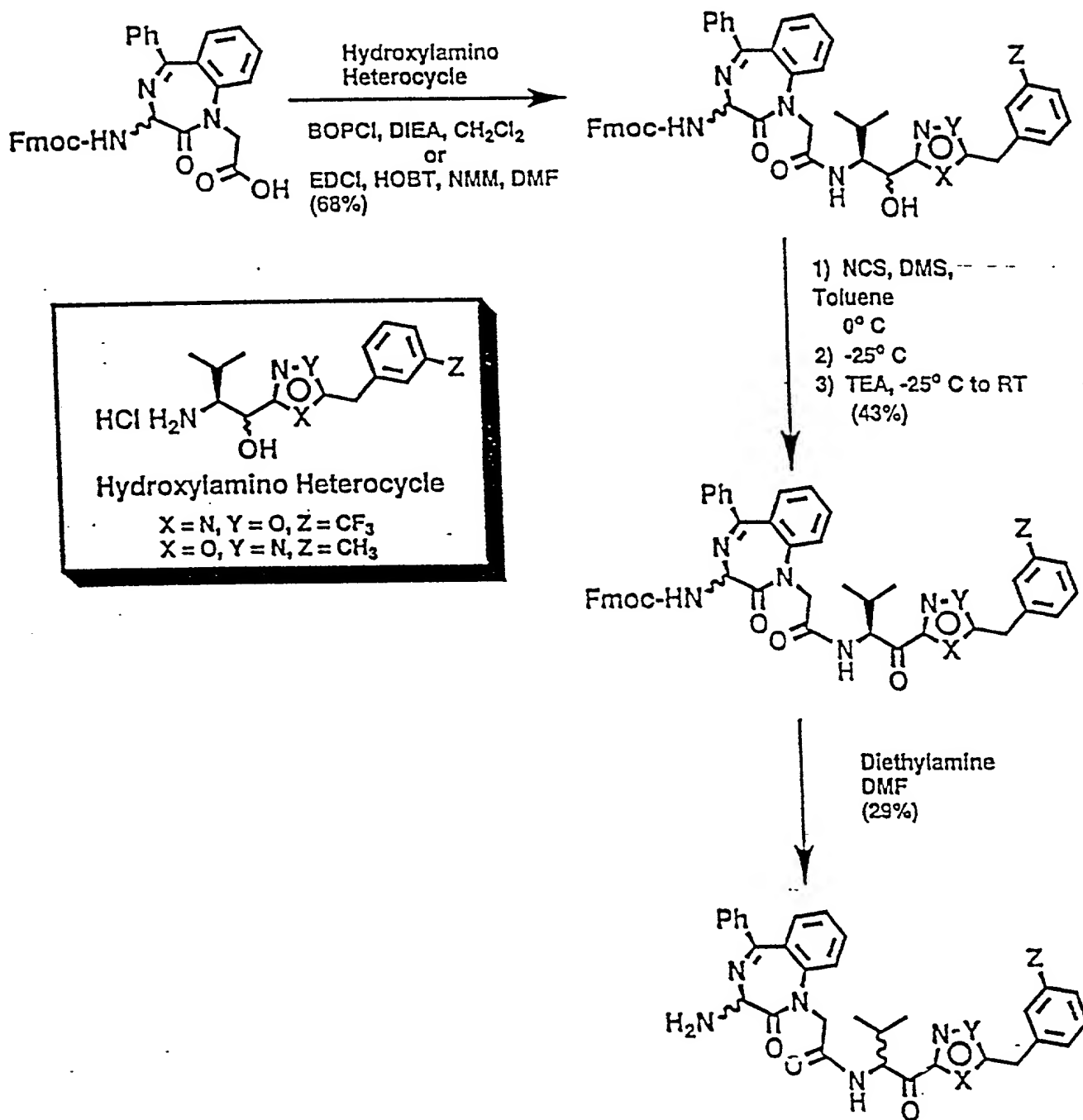


Figure 7

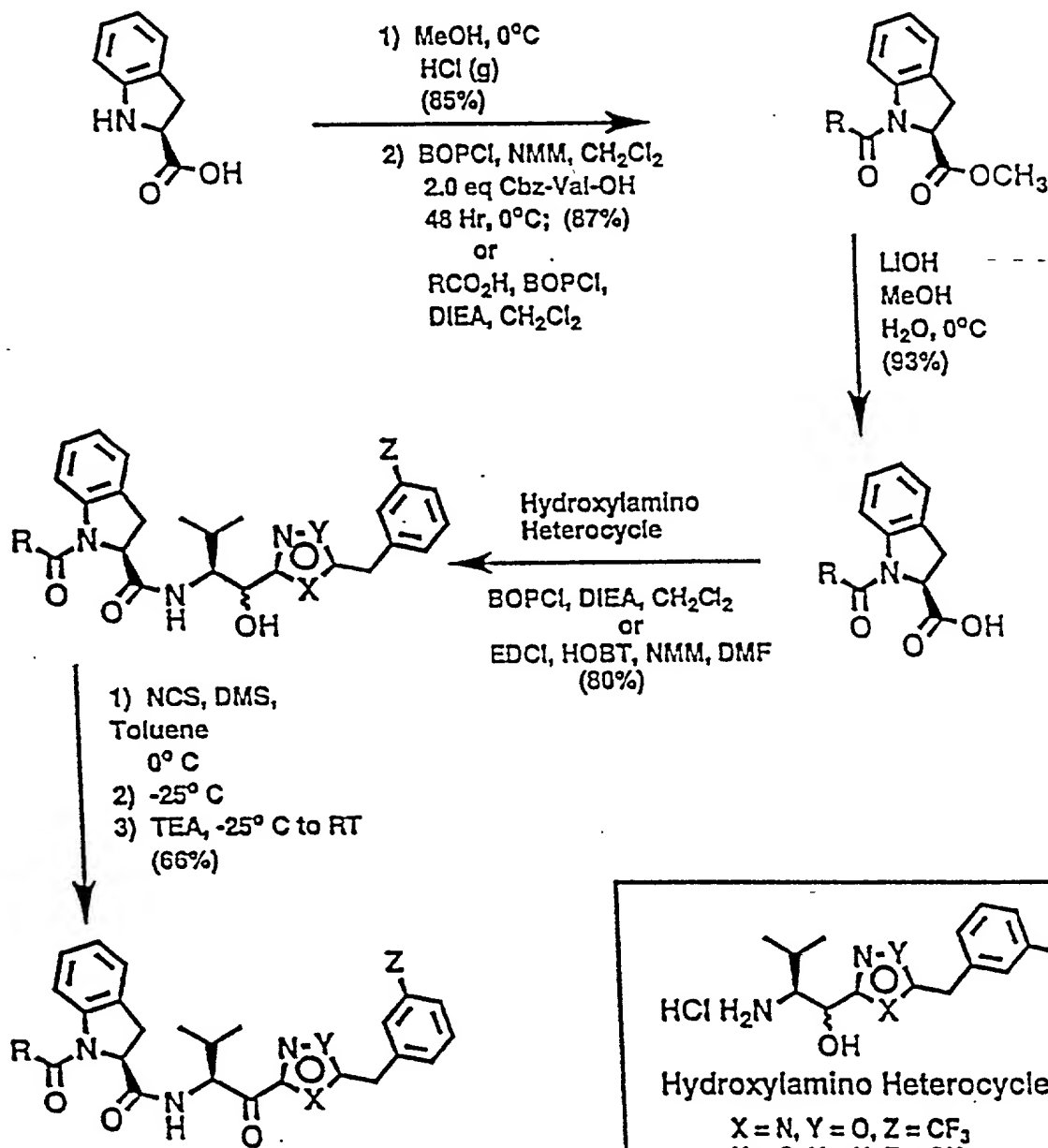
Synthetic Scheme for P₂-P₃ Modified Inhibitors



099233-031001

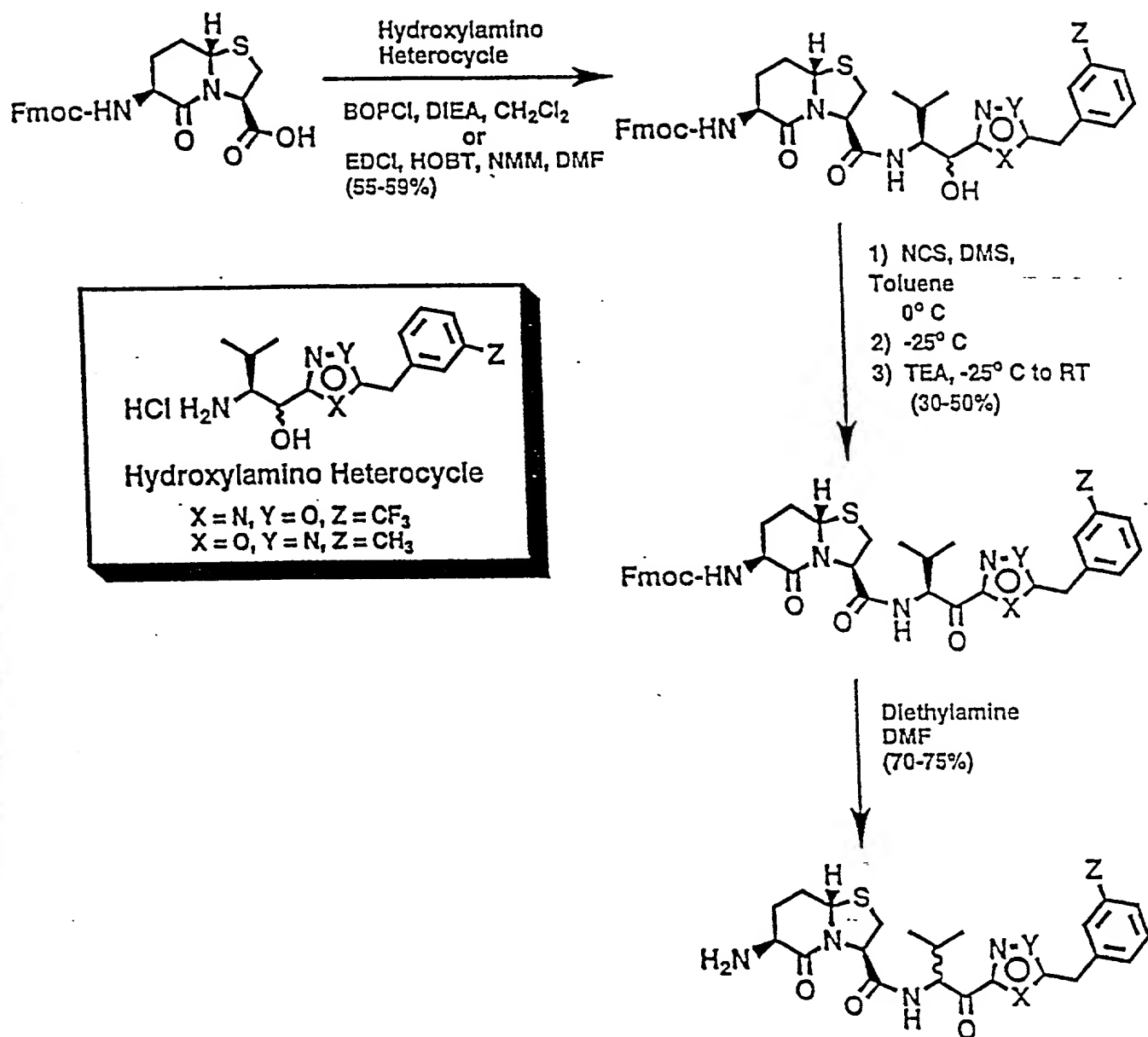
Figure 8

General Synthetic Scheme for P₂-P₃ Modified Inhibitors



T-00180-228/260

Figure 9

Synthetic Scheme for P₂-P₃ Modified Inhibitors

T00790"002660

Figure 10

General Synthetic Scheme for P₂-P₃ Modified Inhibitors

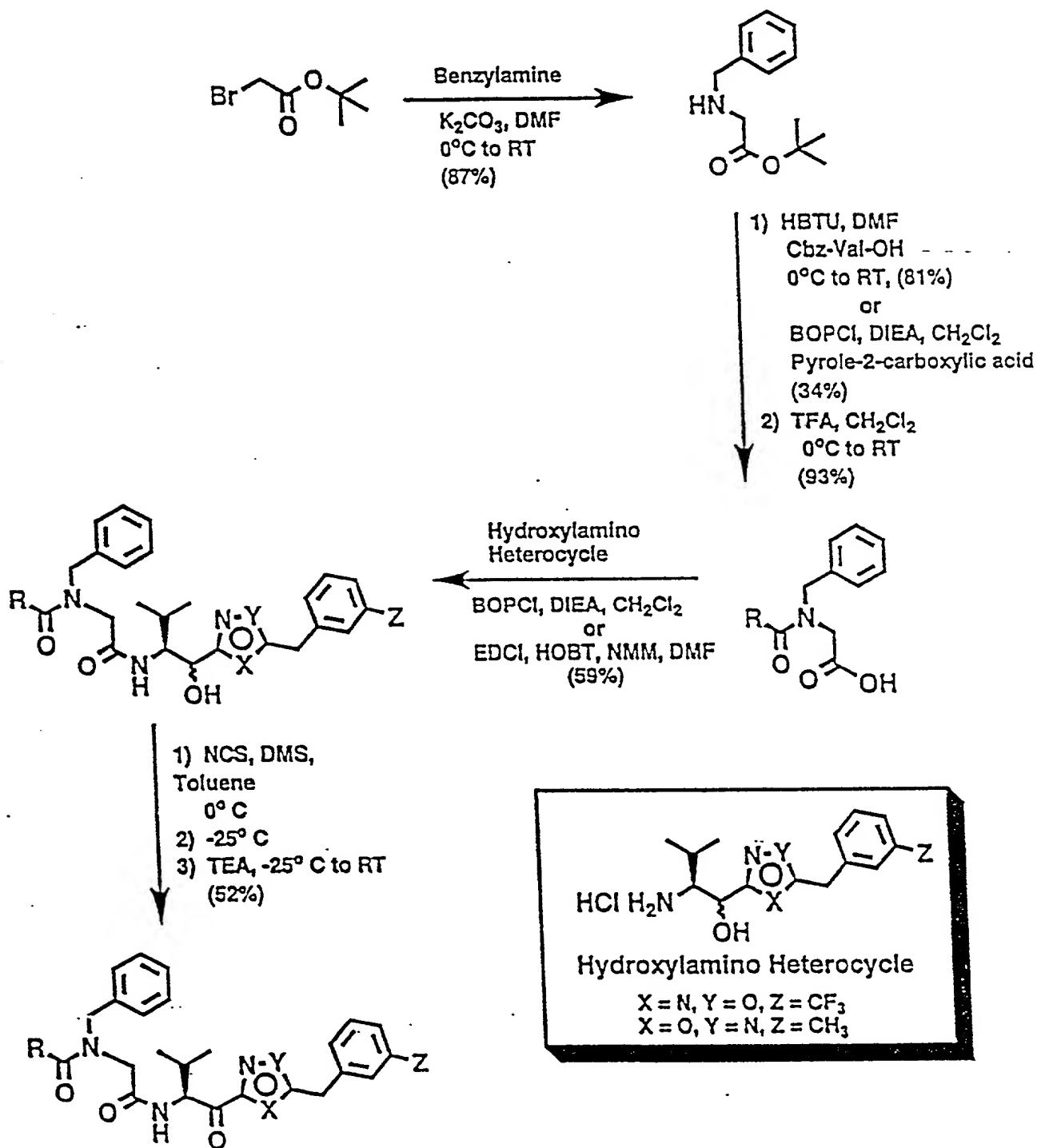


Figure 11

General Synthetic Scheme for P₂-P₃ Lactam Based Inhibitors

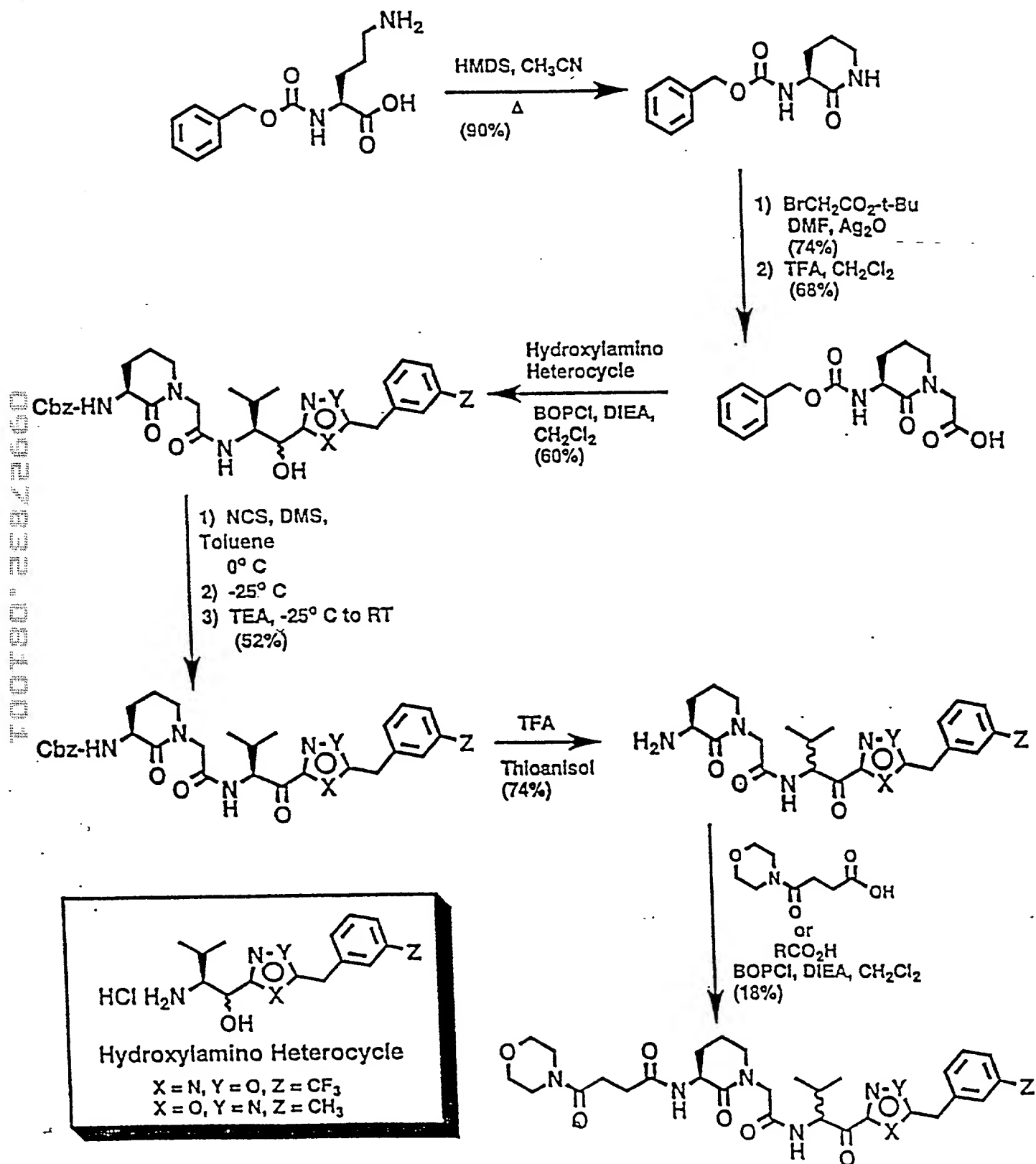


Figure 12

General Synthetic Scheme for P₂-P₃ Lactam Based Inhibitors

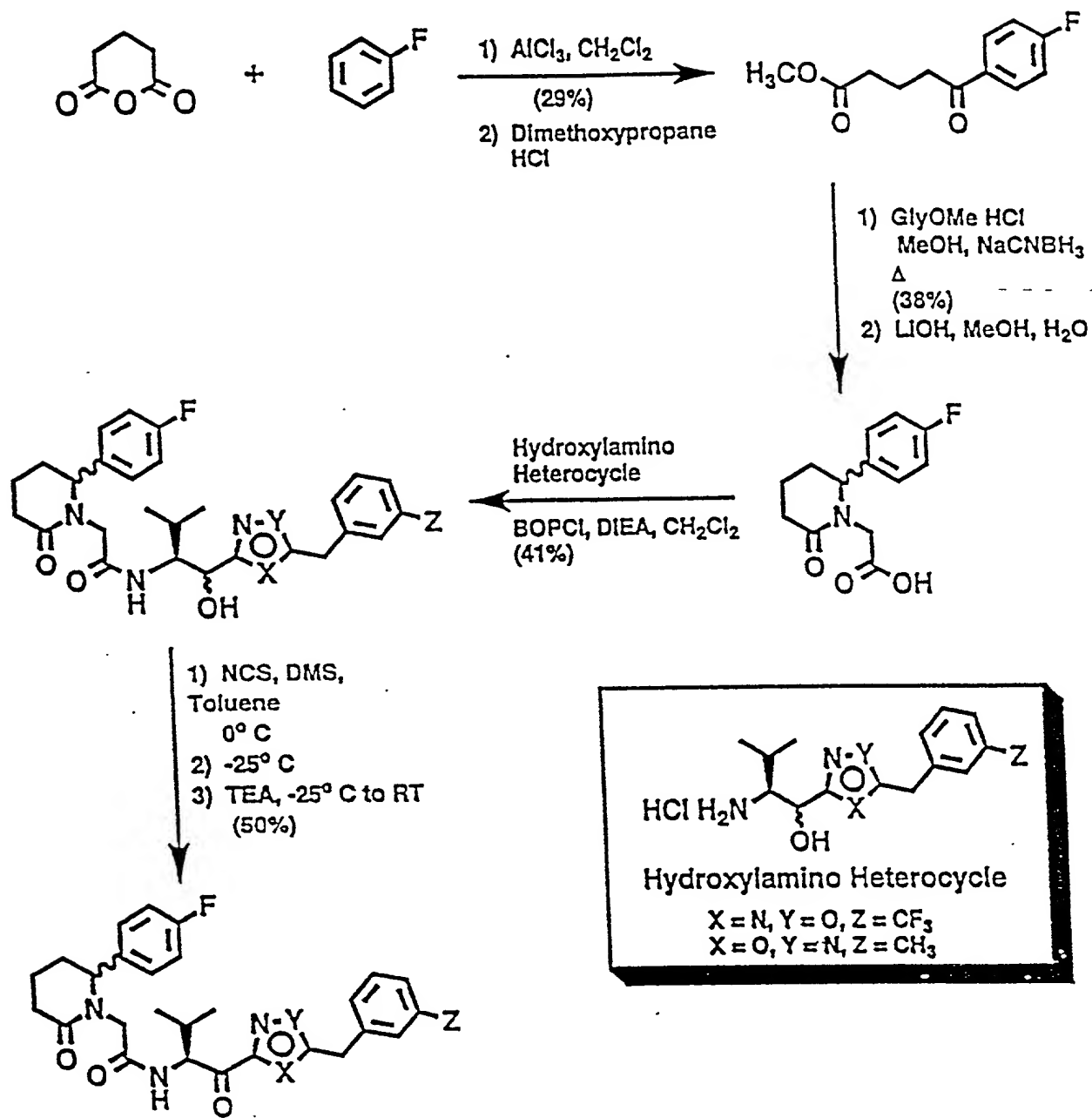


Figure 13

General Synthetic Scheme for Metathiazanone Based Inhibitors

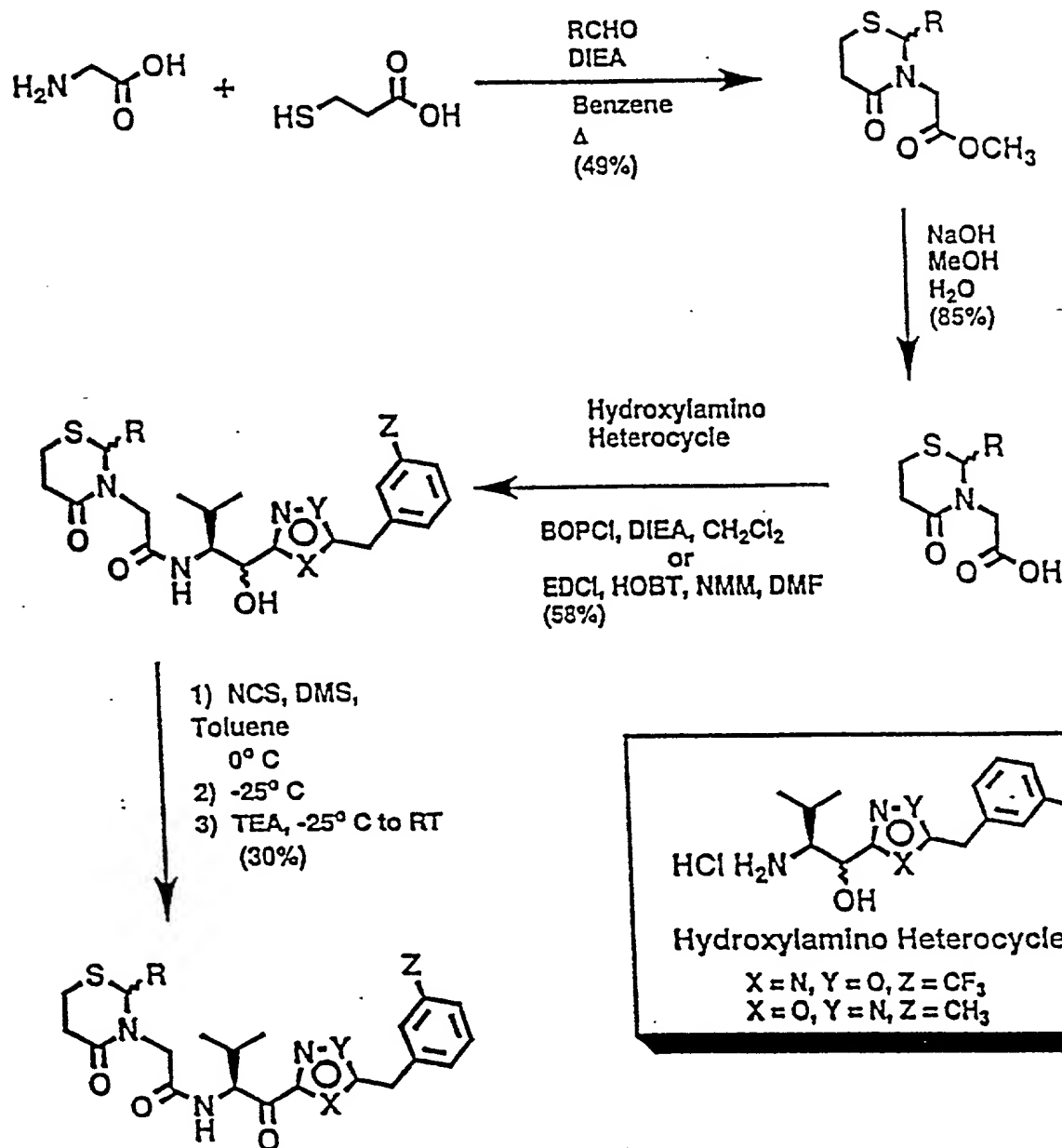


Figure 14

General Synthetic Scheme for Thiazolidinone Based Inhibitors

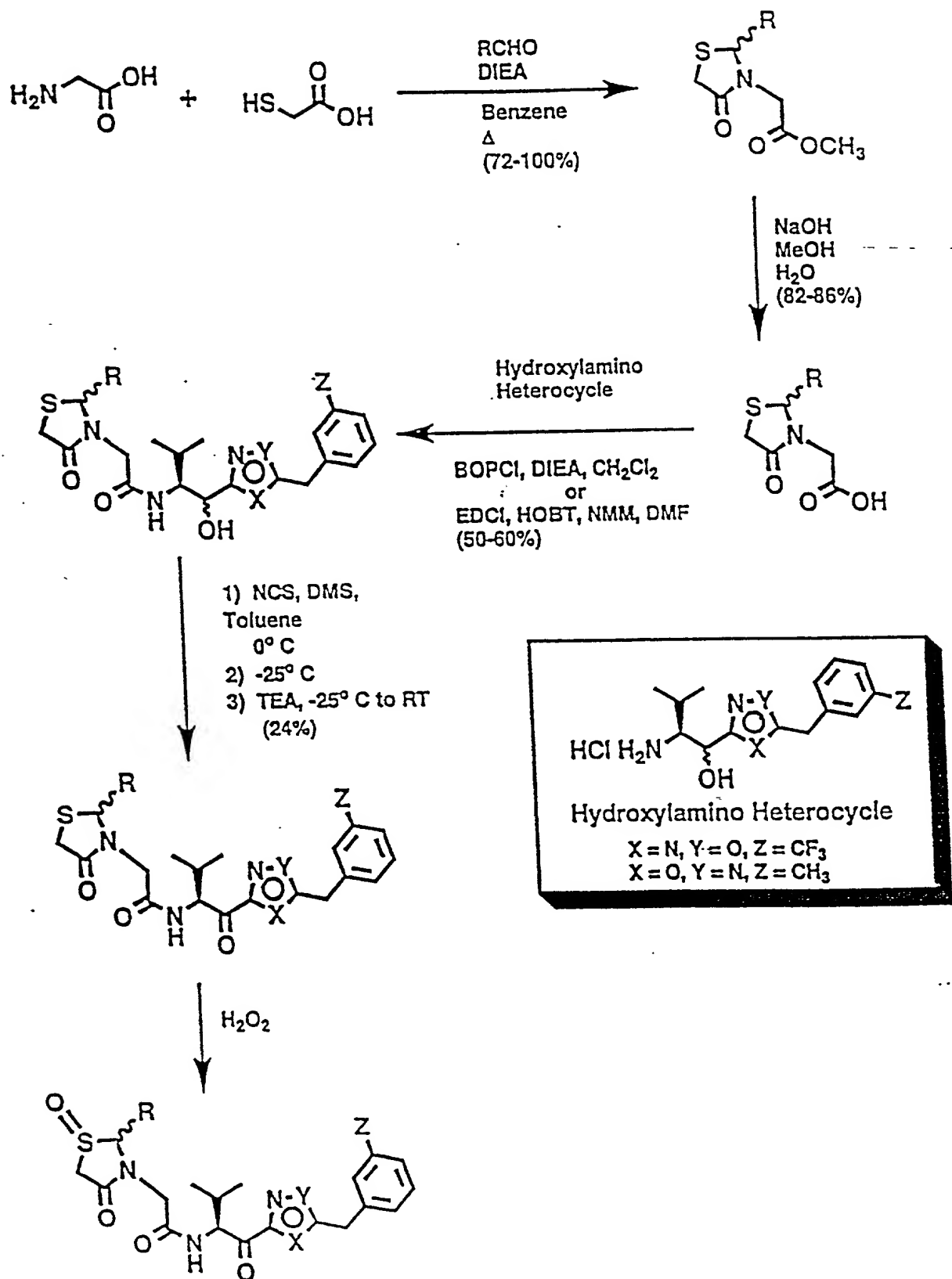


Figure 15

General Synthetic Scheme for Pyridazinedione Based Inhibitors

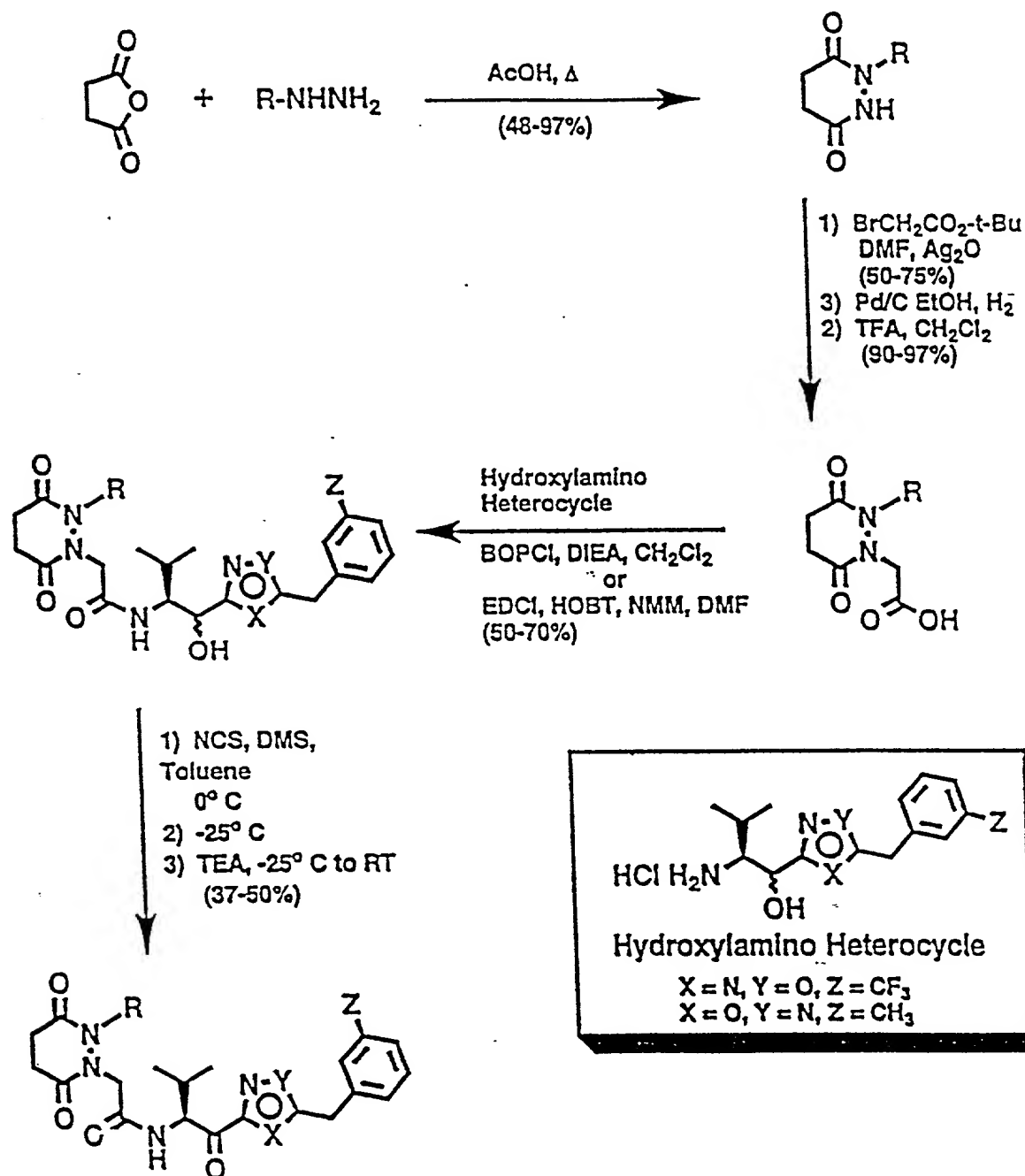
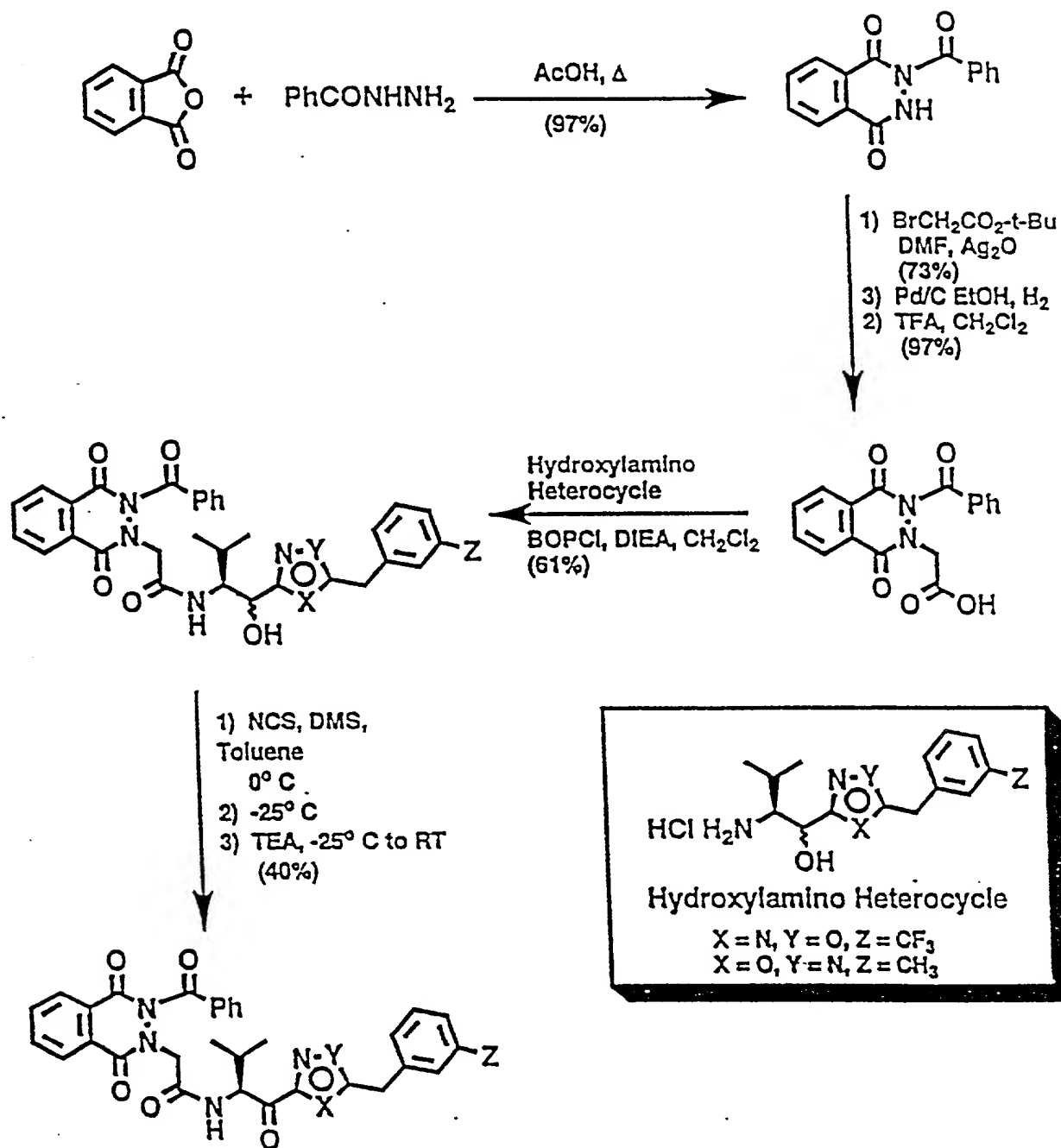


Figure 16

General Synthetic Scheme for Benzopyridazinedione Based Inhibitors



T03429-22942660

Figure 17

General Synthetic Scheme for Quinolone and N-Substituted Quinolone Based Inhibitors

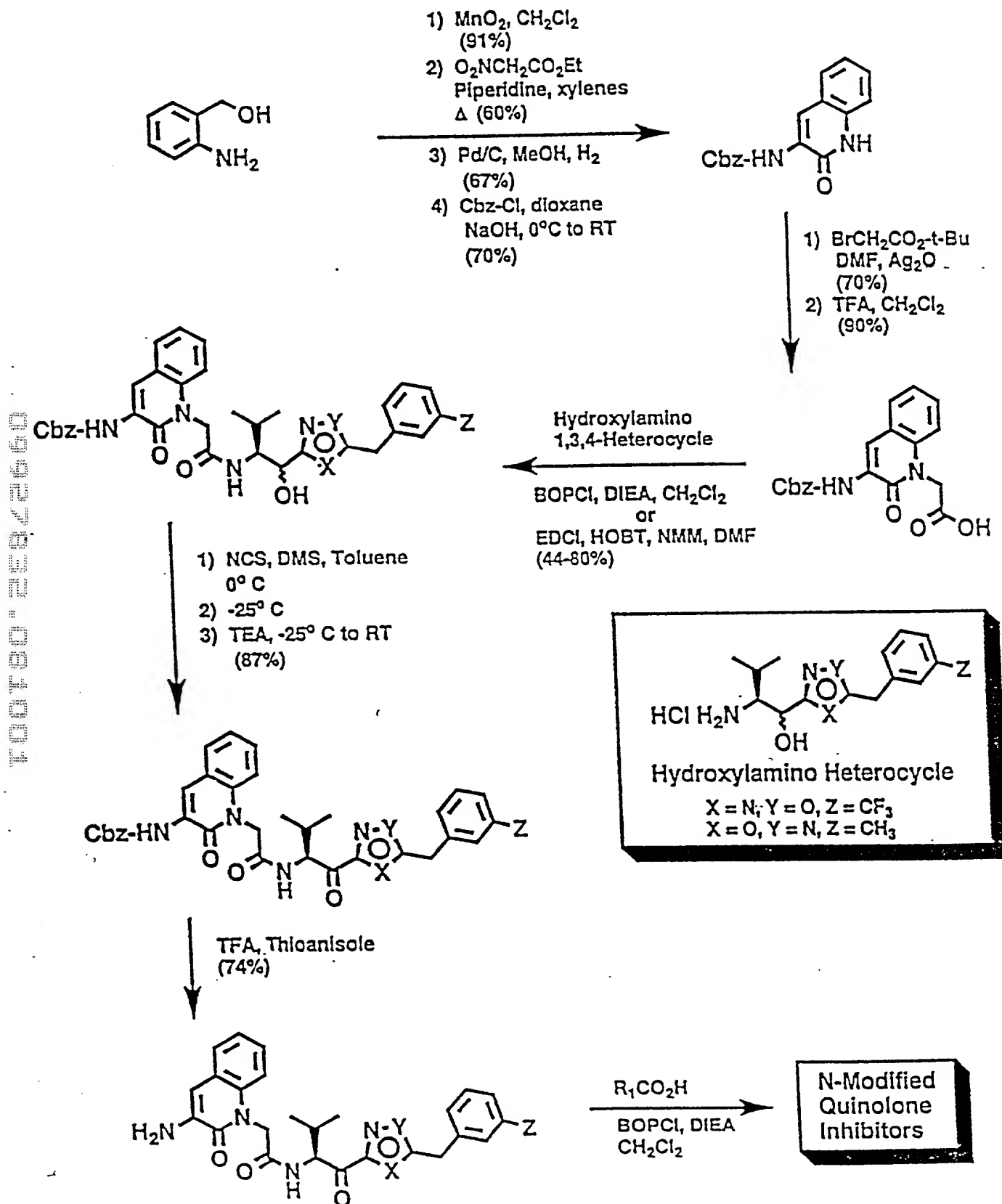
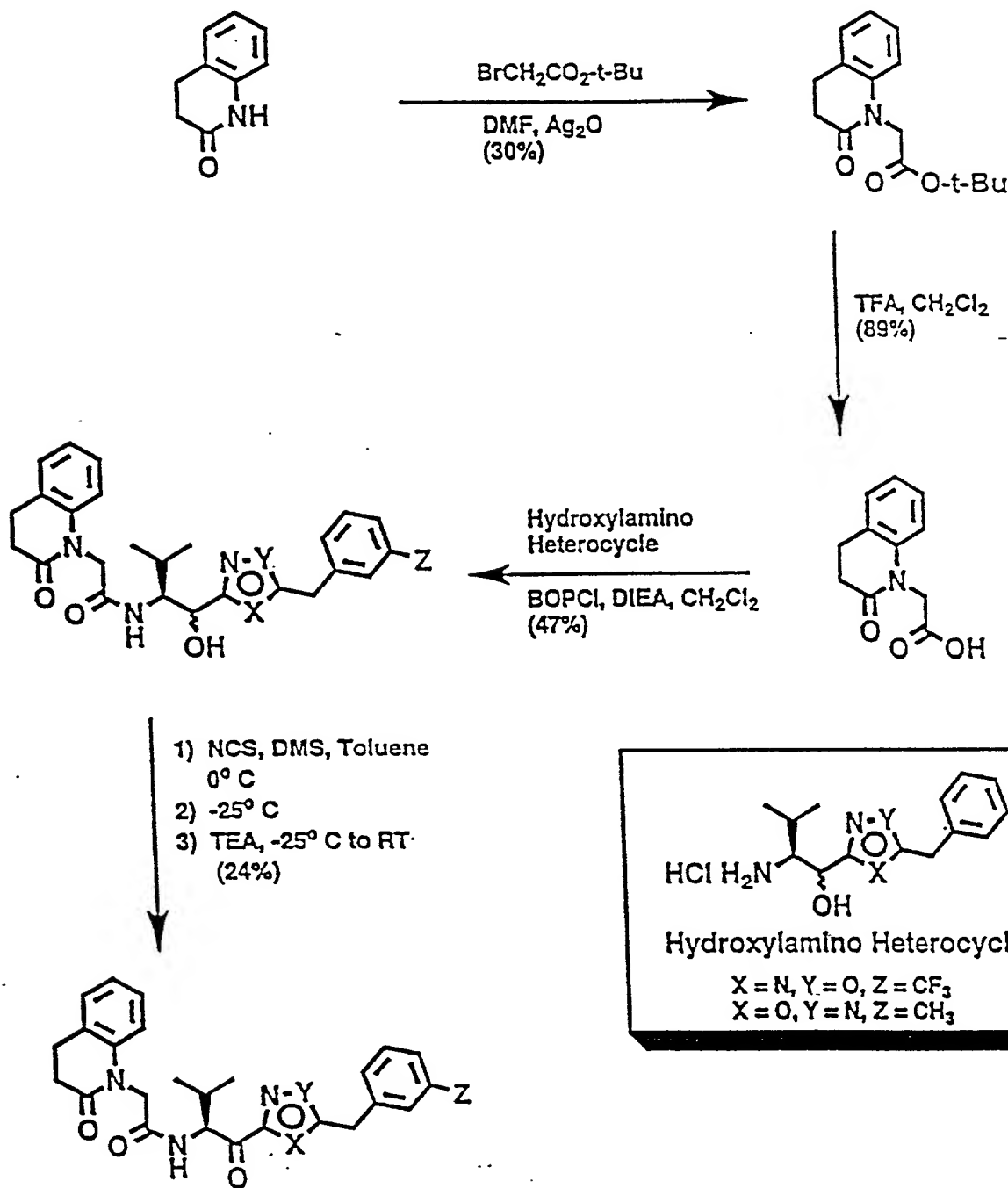


Figure 18

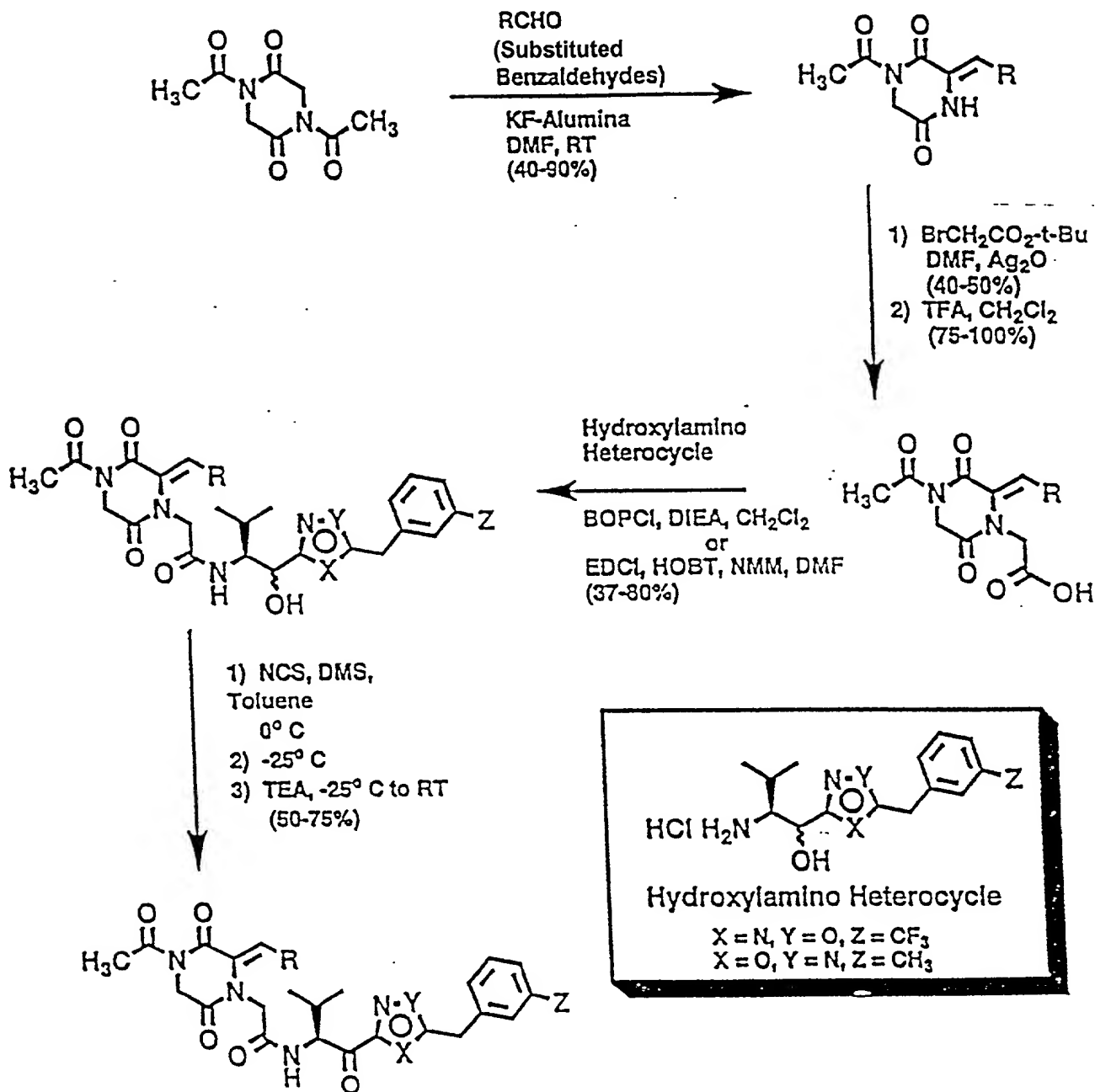
General Synthetic Scheme for 3,4-Dihydroquinolone Based Inhibitors



T00190 22822650 05927832 001001

Figure 19

General Synthetic Scheme for Benzylidene Diketopiperazine Based Inhibitors



T0927832-081084

Figure 20

General Synthetic Scheme for Diketopiperazine Based Inhibitors

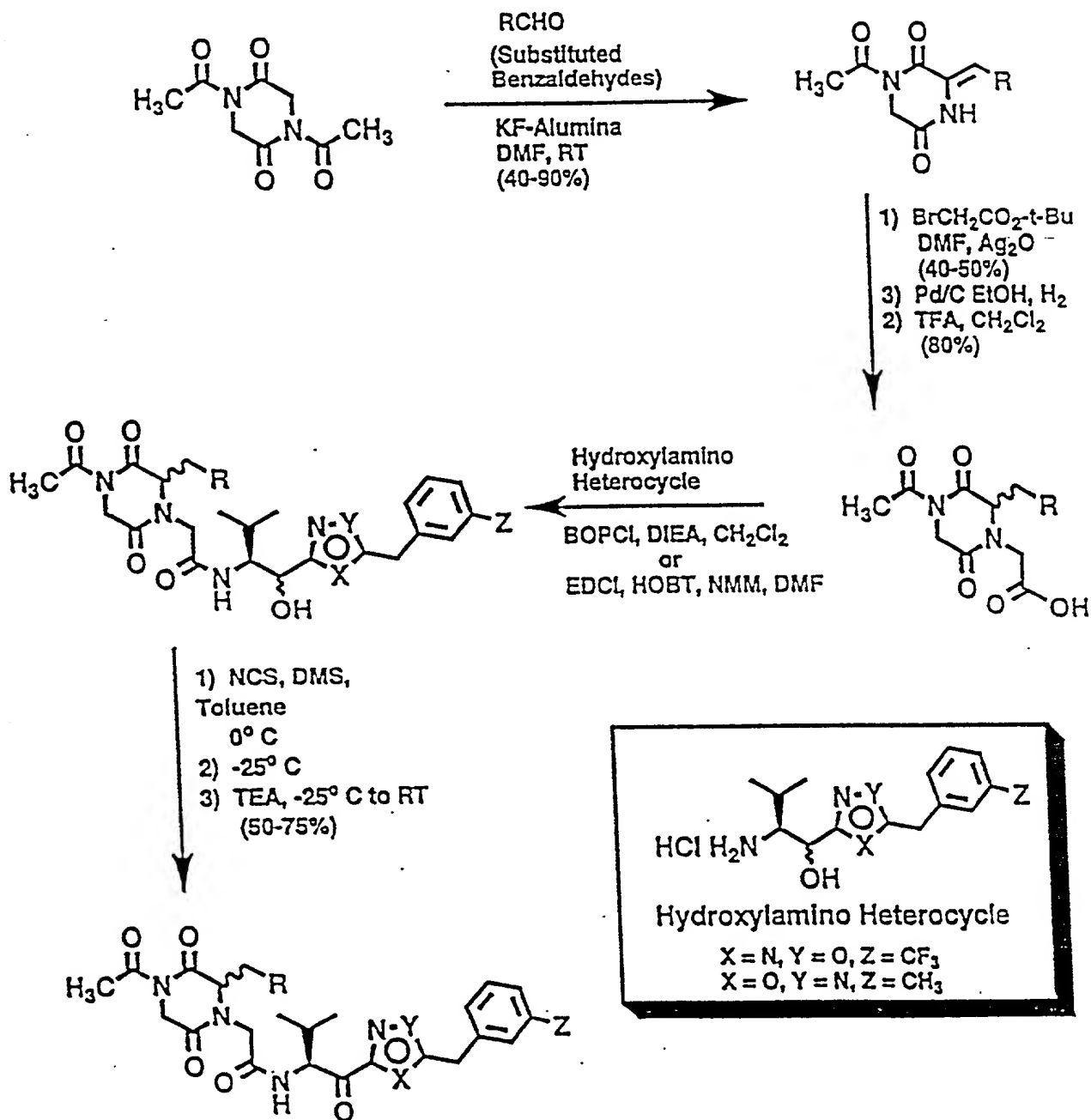


Figure 21

Synthetic Scheme for Hydantoin Based Inhibitors

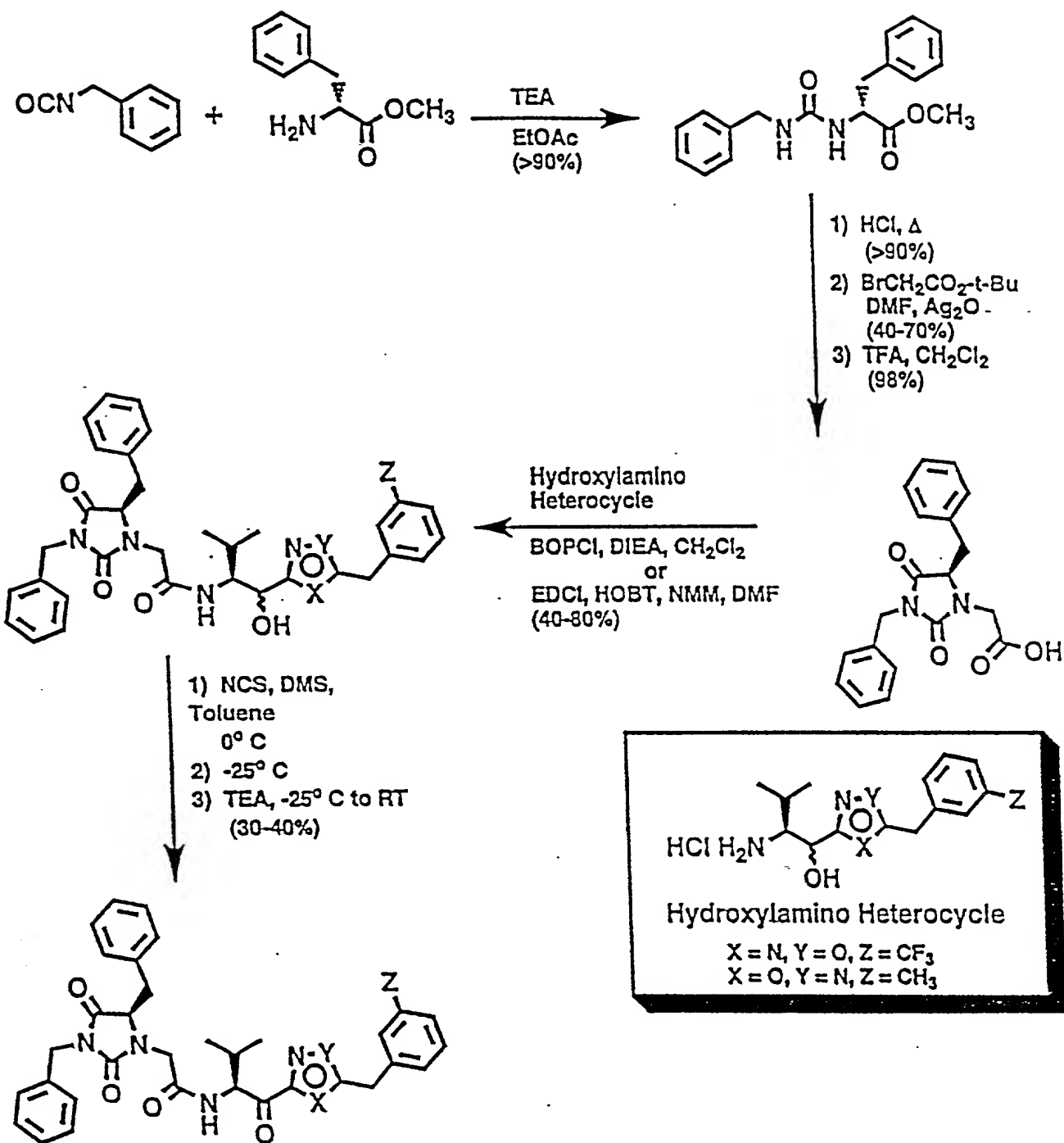


Figure 22

General Synthetic Scheme for Hydantoin Based Inhibitors

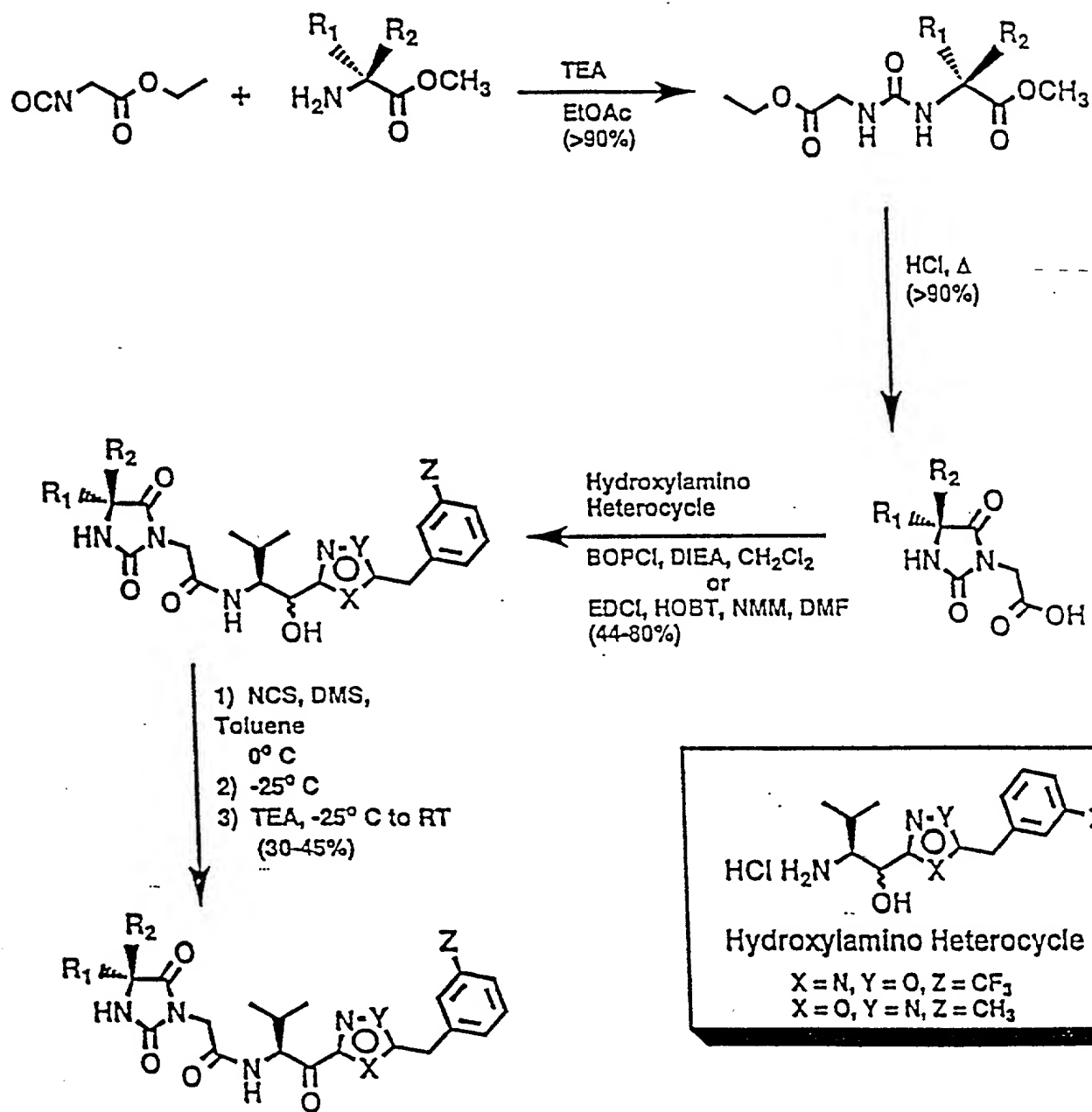
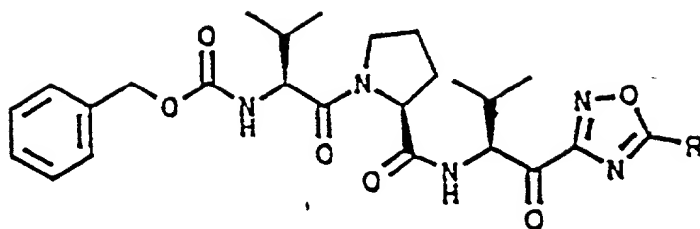


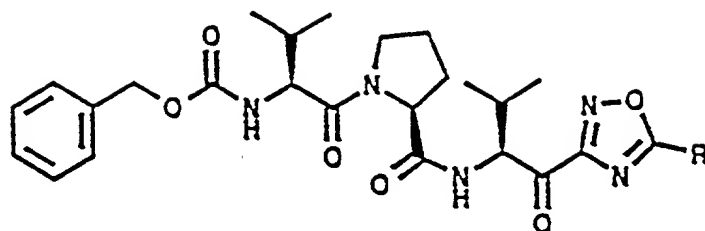
Figure 23



CE#	R	K _i (nM)	CE#	R	K _i (nM)
2039		2.0	2054		0.29
2042		2.5	2055		0.49
2045		1.0	2058		0.56
2048		0.36	2062		0.30
2049		0.5	2066		0.98
2052		0.37	2096		0.8
2053		0.41	2115		1.0

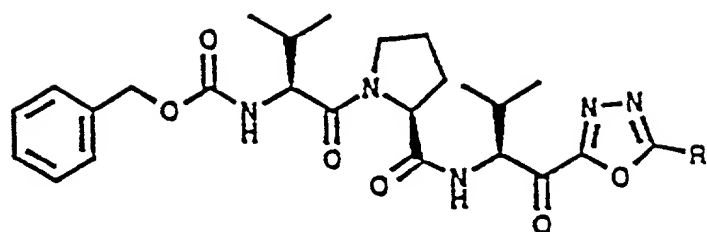
2007-09-28 10:00

Figure 24



CE#	R	K _i (nM)	CE#	R	K _i (nM)
2046		9.9	2077		0.15
2047		3.8	2078		1.05
2050		1.84	2092		6.3
2057		0.38	2103		12.4
2069		4.4	2119		7.7
2073		0.24	2152		0.24
2076		1.46			

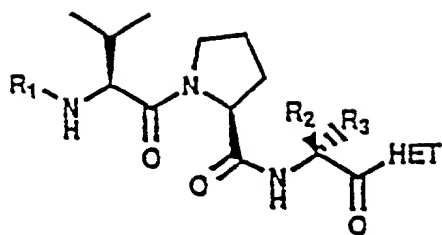
Figure 25



CE#	R	K_I (nM)
2072		0.025
2074	-CH ₃	0.99
2075		0.11
2100		0.069
2123	-N(CH ₃) ₂	15.1
2124		0.033

200780-228/2660

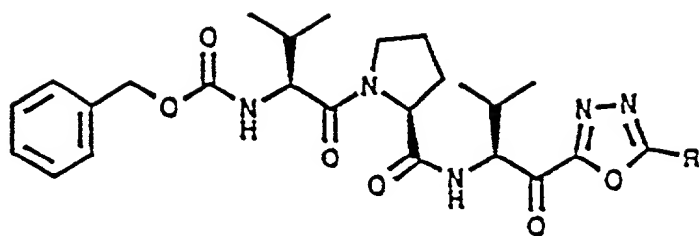
Figure 26



CE#	R ₁	R ₂	R ₃	HET	K _i (nM)
2083	Cbz-	CH ₃	CH ₃		73.0
2098		<i>L</i> -Propyl	H		85.0
2104		<i>L</i> -Propyl	H		0.33
2109		<i>L</i> -Propyl	H		126
2110		<i>L</i> -Propyl	H		0.13

20190729 22:23:25

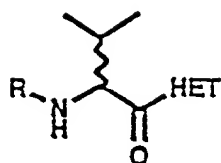
Figure 27



CE#	R	K _i (nM)
2072		0.025
2074	-CH ₃	0.99
2075		0.11
2100		0.069
2123	-N(CH ₃) ₂	15.1
2124		0.033

2007-03-26 14:26:00

Figure 28



CE#	R	HET	K_i (nM)
2130		B	10.0
2132		A	24.0
2134		B	2.0
2135		A	17
2126		B	5.05
2127		A	33.9

Heterocycles:

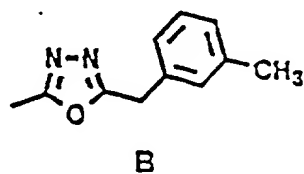
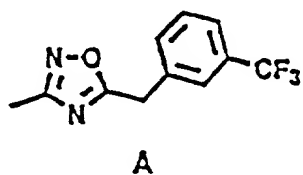
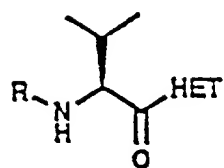
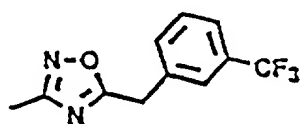


Figure 29

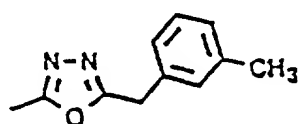


CE#	R	HET	K_i (nM)
2125		A	0.40
2145		B	0.038
2143		A	25.0
2056		A	0.98
2097		A	60.0
2156		A	512.0

Heterocycles:

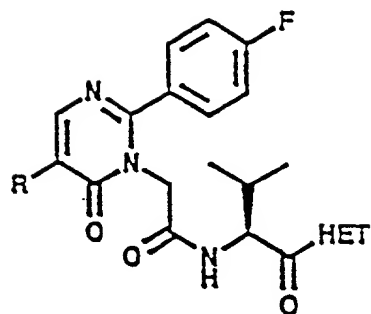


A



B

Figure 30



CE#	R	HET	K_i (nM)
2089	Cbz-NH-	A	1.5
2090	NH ₂ -	A	2.7
2095	Cbz-NH-	B	0.21
2101	NH ₂ -	B	0.64

Heterocycles:

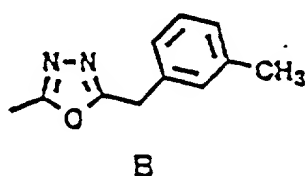
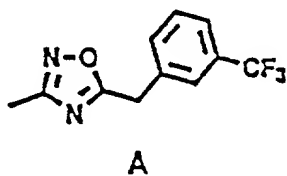
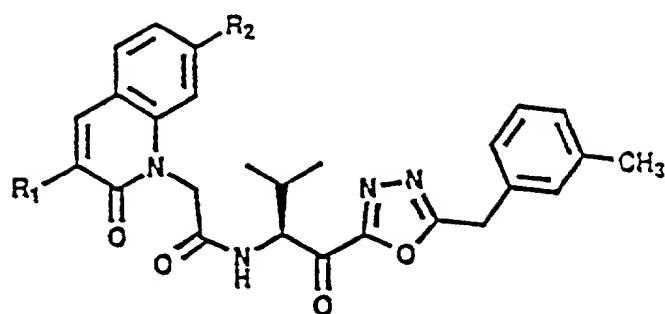
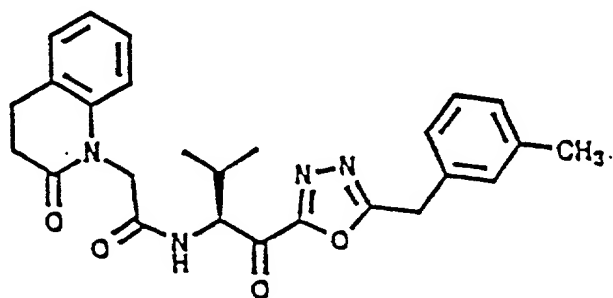


Figure 31

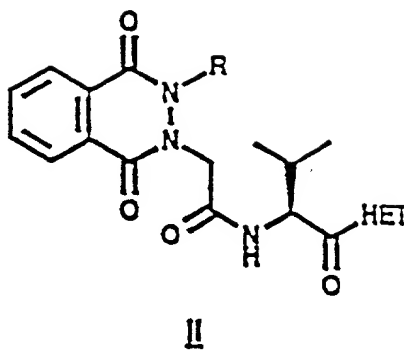
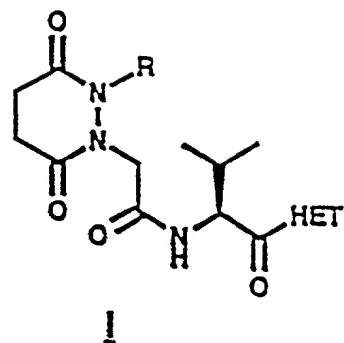


CE#	R_1	R_2	K_i (nM)
2107	Cbz-NH-		17.0
2108	Cbz-NH-	H	10.5
2113	H ₂ N-	H	38.8
2116		H	76.3
2117		F	587.0



CE-2088 $K_i = 66.0$ nM

Figure 32



CE#	R	Structure	HET	K_I (nM)
2138		I	B	294.0
2147		I	B	1590
2148		I	A	>6000
2140		II	B	204.4

Heterocycles:

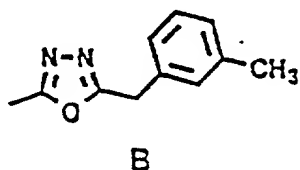
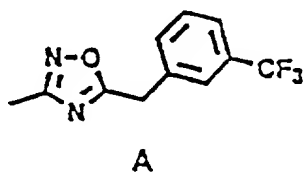
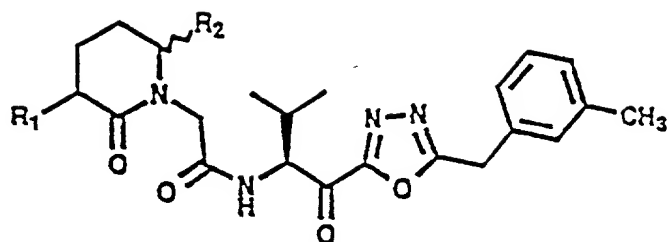

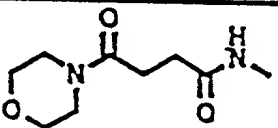


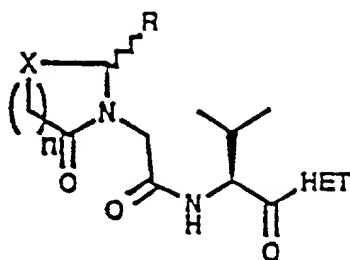
Figure 33



CE#	R ₁	R ₂	K _i (nM)
2079	Cbz-NH-	H	35.5
2080	H ₂ N-	H	62.0
2087	H		19.8
2091		H	270.0

200703-282366

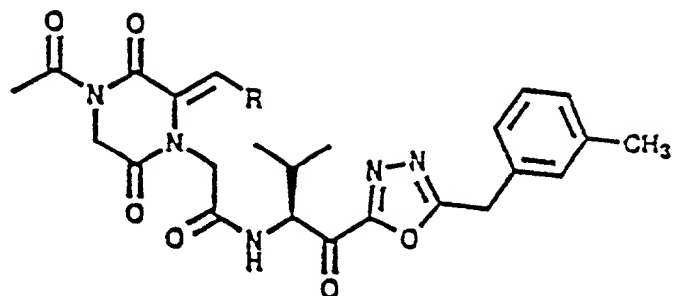
Figure 34


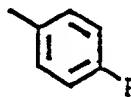
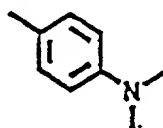
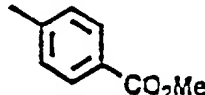
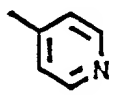


CE#	n	X	HET	R	K_i (nM)
2118	2	S			13.2
2121	1	S			28.0
2122	1	S			62.7
2136	1	SO			104.0
2137	1	SO			557.0

TOP SECRET 222660

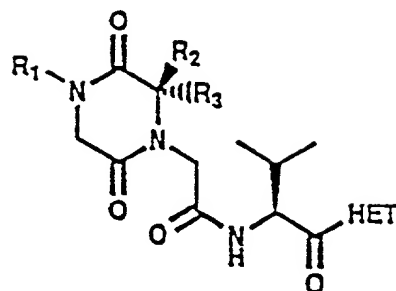
Figure 35



CE#	R	K_i (nM)
2099		1.9
2105		0.72
2111		20.1
2112		1.17
2114		25.1

2099 2105 2111 2112 2114

Figure 36



CE#	R ₁	R ₂	R ₃	HET	K _i (nM)
2084	CH ₃			A	133.0
2106	CH ₃			B	40.7
2120	CH ₃ CO-			B	50.9
2128		-H		B	64.0
2129		-H		A	300.3
2133		-H		C	33200
2139	H-			B	41.0
2144			-H	B	9.3
2146			-H	A	67.3

Heterocycles:

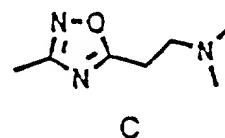
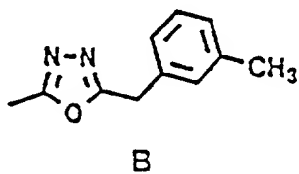
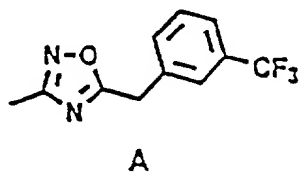
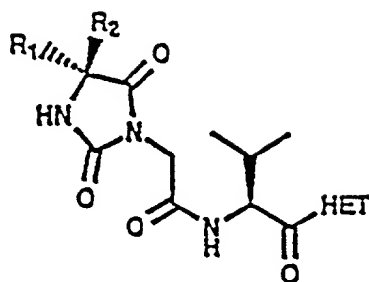


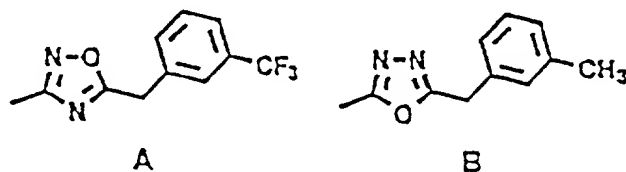
Figure 37

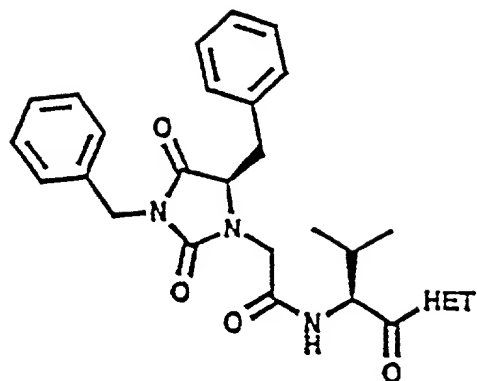


CE#	R ₁	R ₂	HET	K _i (nM)
2141		H	A	64.0
2142		H	B	8.7
2149 ^{**}		H	B	0.28
2154	H		B	10.0
2155	H		A	57.0

^{**} Stereochemistry not definitive

Heterocycles:



[illegible]

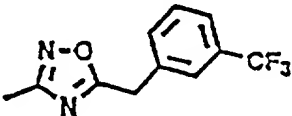
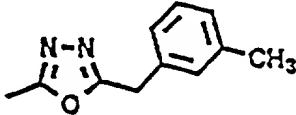
CE#	HET	K _I (nM)
2150		>1000
2151		60

Fig - Synthesis of ONO-PO series compounds

